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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/521,295	05/17/2005	Aleksander Resman	RG/G-33025A/Lek	9703

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Lek (Slovenia) - LUEDEKA, NEELY & GRAHAM, P.C.
P.O. BOX 1871
Knoxville, TN 37901

EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
12/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/521,295	RESMAN ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/13/10*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-9,13-18 and 20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-9,13-18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/13/10 has been entered.

Claims 6, 10-12 and 19 have been cancelled. Claims 1-5, 7-9, 13-18 and 20 are pending and under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 5/13/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn. Claims 1-5, 7-9 and 12-18 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. Applicant has deleted "at least about 90%". The rejection is withdrawn. Claim 18 was rejected under 35 U.S.C. 112, first paragraph. Applicant has deleted 'prevention' and the rejection is withdrawn.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-5, 7-9 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 introduces new matter as the claim recites the limitation: "about 2.5%" There is no support in the specification for this limitation. The limitation of: "about 2.5%" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The specification discloses "up to a desired humidity grade, e.g. 2.5%" in [0025] but does not describe the instantly claimed limitation. There is no guidance in the specification to select "about 2.5%" and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant has not directed the Examiner to the support in the specification for the amendments. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

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> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 20 introduces new matter as the claim recites the limitation: "at least 10% of a second film-forming agent" There is no support in the specification for this limitation. The limitation of: "at least 10% of a second film-forming agent " was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. There is no guidance in the specification to select "at least 10% of a second film-forming agent" and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant has not directed the Examiner to the support in the specification for the amendments. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

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Claims 17 and 18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 17 and 18 introduce new matter as the claims recite the limitation: "a capsule" There is no support in the specification for this limitation. The limitation of: "a capsule" was not described in the specification as filed, and person skilled in the art would not recognize in the applicant's disclosure a description of the invention as presently claimed. The plain and ordinary meaning of 'capsule' in the pharmaceutical arts is a liquid or solid dosage form in which the drug is enclosed in a hard or soft soluble container. This is not disclosed in the specification as filed. The specification discloses "encapsulating" on page 6 but does not describe the instantly claimed limitation. Simply because something is encapsulated does not necessarily mean that a capsule is present. A tablet can be encapsulated with an enteric coating, for example. There is no guidance in the specification to select "a capsule" and from MPEP 2163.06: "Applicant should therefore specifically point out the support for any amendments made to the disclosure." Applicant directed the Examiner

to the support in the specification on page 6 for the amendments but support has not been found. Therefore, it is the Examiner's position that the disclosure does not reasonably convey that the inventor had possession of the subject matter of the amendment at the time of filing of the instant application.

Response to arguments:

Applicant states that these rejections are not well taken and alleges that the specification clearly indicates that the micronized clarithromycin particles may be incorporated into either a tablet or a capsule. Respectfully, the Examiner cannot agree. The term 'capsule' is not present. The term 'encapsulating' is used with respect to a mixture and not a 'capsule' for administration as Applicant would have the Examiner believe. See [0034] (Examiner added emphasis): "The pre-treated clarithromycin is the starting material for a direct tabletting or ***encapsulating mixture***, where during the compression process itself a matrix is formed…". Clearly, the 'encapsulating' is not placing the clarithromycin in a capsule but rather blending it with some mixture for compression to form a matrix. The concept of making 'capsules' in the pharmaceutical sense is absent and the process of 'encapsulting' does not provide support for a 'capsule' as discussed above in detail. If Applicant had intended to make capsules then Applicant should have disclosed capsules.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-7, 14-16 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 4, 5 and 16 recite “over about". Claim 7 recites: "under about". Claims 14, 15, and 20 recite: “up to about”. The terms “over”, “under” and “up to” provide static endpoints of a value. In contrast the term “about” provides variability around a value. The value cannot be simultaneously static and dynamic. The Examiner suggests amending to the alternative. For example: "...over X or about X...".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-5, 7-9, 13-18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Broad et al. US 5705190 in view of Ansel et al. (Pharmaceutical

Dosage Forms and Drug Delivery Systems 7th Edition, 1999, Lippincott Williams & Wilkins, NY, pages 91, 108, 209-211 and 221-223) and Kirschner et al. (US 6899890) and Yonemochi et al. (European Journal of Pharmaceutical Sciences, 1999, (7), 331-338) and Pollock et al. (27th International Symposium on Controlled Release of Bioactive Materials July 2000; 4 pages).

Applicant claims:

Claim 1. (Currently Amended) A method for a physical pre-treatment of an active substance to provide cores, characterized in that it comprises adding a poor solvent or a mixture of solvents to the active substance or to a mixture of the active substance with one or more excipients, the solubility of the substance in said solvent being less than 0.1 g/L, followed by drying to a final humidity of about 2.5%, wherein the active substance comprises micronized clarithromycin, wherein ~~at least about 90% of~~ the micronized clarithromycin particles ~~are~~ have a particle size d(0.9) of about 30μm ~~or less in size~~ and enter a direct mixture for tabletting or encapsulating.

Determination of the scope and content of the prior art

(MPEP 2141.01)

Broad et al. teaches composition and methods of making tablets of clarithromycin (Example 1 and claims 15-17). Broad et al. teach sparingly soluble drugs such as clarithromycin (which is intrinsically difficult to be directly tabletted or encapsulated and brittle and/or porous) which has a solubility of about 1 part in 1000 part of water which the Examiner interprets to mean practically insoluble (Abstract; column 1, lines 5-10; column 2, lines 46-59; and column 3, lines 38-40). The amount of drug can vary from

about 40 to 75% of the total tablet (column 3, lines 63-65). Since Broad et al. teach clarithromycin, then all sizes and percentages of clarithromycin within those sizes are embraced by the teachings of Broad et al. Dry blending of ingredients followed by wet granulation with an aqueous solution (water is a poor solvent), drying, and tabletting is taught which reads on instant claim 13 (see example 1, column 5, for example). Since the same ingredients are used then pores are intrinsically formed. The presence of water intrinsically humidifies the composition. Excipients are taught such as diluents, binders, glidants, bulking agents and coating materials (column 5, lines 1-10). Compositions can be coated (column 5, lines 11-14).

Ansel et al. teach why one of ordinary skill in the art would micronize poorly soluble drugs which is to enhance the rate of dissolution (page 108, right column); how to make tablets through a wet granulation process which introduces water and intrinsically humidifies the ingredients (pages 209-211); teach aqueous film forming coating agents such as hydroxyethyl cellulose and hydroxypropyl methylcellulose (the same material used by applicant: see instant specification page 10, example 5) (page 91, table 3.3; and pages 221-223). Since the agents are the same as instantly claimed then they intrinsically have the same viscosity in the absence of evidence to the contrary.

Kirschner et al. teach micronized therapeutically active drug, such as clarithromycin, with a particle size ranging from about 0.1 microns to less than 60 microns in a tablet (Claims 1-5, 9, 13 and column 14, line 53).

Yonemochi et al. teach that high humidity can lead to structural changes in clarithromycin during processing (Abstract and Figure 6).

Pollock et al. teach using 15 cps, which is 15 mPas viscosity, HPMC for producing film coatings on tablets for controlled release of active agents (Page 1, background; page 3, left column and conclusions and Figures 1-4). Pollock et al. teach that the drug release can be controlled by the level of the HPMC in the compression coating in addition to the chemistry or viscosity grade (page 3, left column). The swelling of the HPMC opens up channels, pores, such that the media can travel into the core and accelerate dissolution of the drug (page 3, upper left column).

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Broad et al. is that Broad et al. do not expressly teach micronizing the clarithromycin to a particle size of where at least 90% of the micronized clarithromycin particles are about 30 μm or less in size and drying to a final humidity of about 2.5%. This deficiency in Broad et al. is cured by the teachings of Ansel et al. and Kirschner et al. and Yonemochi et al.

2. The difference between the instant application and Broad et al. is that Broad et al. do not expressly teach a polymer in the coating with the recited viscosity values or more than one coating agent on a clarithromycin tablet of instant claim 20. This deficiency in Broad et al. is cured by the teachings of Ansel et al. and Pollock et al.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to micronize the clarithromycin to a particle size of where at least 90% of the micronized clarithromycin particles are about 30 μm or less in size and drying to a final humidity of about 2.5% of Broad et al., as suggested by Ansel et al. and Kirschner et al. and Yonemochi et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because it is known that clarithromycin is sparingly soluble and Ansel et al. teach that to increase the rate dissolution one of ordinary skill in the art can micronize the drug. The disclosure of Broad et al. embraces all forms and sizes of clarithromycin and Kirschner et al. provide guidance on the proper particle size to use in tablets and in the absence of evidence to the contrary all of the particles, 100% can be within the instantly claimed size. Furthermore, Yonemochi et al. teach that high humidity can result in structural changes of clarithromycin and therefore it is desirable for the ordinary artisan to avoid high humidity and seek low or no humidity to avoid those structural changes during drying. A final humidity of 2.5% is merely routine optimization by the ordinary artisan in the absence of evidence to the contrary.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add a polymer in the coating of Broad et al. with the recited viscosity values or more than one coating agent of instant claim 20, as suggested by Ansel et al. and Pollock et al., and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Broad et al. teach adding a coating and Ansel et al. teach the same polymers to use for the coating. Pollock et al. further teach that modifying the viscosity results in different release rates of the drug and teaches using 15 cps which is 15 mPas for rapid release with respect to HPMC that does not swell at all (Figures 2 and 3). Thus, the ordinary artisan would select lower viscosity HPMC to provide faster release of the drug. It is merely judicious selection of one or more of the known coating polymers taught by Ansel et al. with the viscosity, as suggested by Pollock et al., and amount instantly claimed by one of ordinary skill in the art in the absence of evidence to the contrary. Furthermore, granulation techniques are well known in the art as taught by Ansel et al. and the products can be then film coated as taught by Ansel et al. and discussed above.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant's arguments are moot in view of the new grounds of rejection.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERNST V. ARNOLD whose telephone number is (571)272-8509. The examiner can normally be reached on M-F 7:15-4:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brian Kwon can be reached on 571-272-0581. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ernst V Arnold/
Primary Examiner, Art Unit 1613